Vaccine Cell Substrates: Bovine and Porcine Virus Considerations

Stephen Wessman
USDA,APHIS,VS
Center for Veterinary Biologics
Ames, Iowa USA

Introduction

Substrate contamination sources

- Serum
- Cells
- Viruses
- Ingredients

Types of contamination

Viruses

Bacteria

Mycoplasma

Fungus

Cells

Cell lines reported as susceptible to bovine viral diarrhea virus

Bovine turbinates
Madin-Darby bovine kidney(MDBK)
Bovine kidney-primary & continuous
Bovine lung
Bovine trachea
Bovine aortic endothelium
Bovine testis
Sheep choroid plexus
Lamb kidney
Ovine turbinates
Monkey kidney (Vero and others)
Bighorn sheep kidney
Chick embryo fibroblasts

Porcine kidney (PK-15,others)
Minipig kidney
Swine testis
Goat kidney
Goat esophagus
Rabbit kidney (RK-13)
Cat lung
Crandell feline kidney (CRFK)
Cat tongue
Feline embryo
Mosquito cells
Chinese hamster ovary (CHO)
Others

9CFR Testing

113.52 Requirements for ingredients of animal origin

- Mycoplasma, bacteria, fungi
- Growth on monolayers at 15% v/v
  - 21 days, at least 2 passes, examined for CPE
  - Cytopathogenic and hemadsorption tests
  - Fluorescent antibody stain for extraneous agents

9 CFR 113.47 Testing

- All cells: BVD, reovirus , rabies
- Bovine, goat,ovine: BT,BoAd,Bopar,BRSV
- Canine: CCV, CDV,CPV,(ICH, BT)
- Equine: EqHerpes, EVA,(BT)
- Feline: FIP,FPV,(FelCor, BT)
- Porcine: SwAd,PPV,TGE,HEV (BT,Rota, PRRS,PRV,SwEnceph,SwineFlu)

Serum Testing at CVB

	1985-1990	1990-1997	1999	2000	2001	2003
Number Tested	2224	6318	34	483	327	881
Number Antibody Positive	853	1320	0	112	36	189
Percent Antibody Positive	38	21	0	23	11	21
Number Virus Positive	61	1673	13	250	107	354
Percent Virus Positive	37	27	38	52	33	40
Total Rejected	1097	2993	13	362	143	543
Percent Rejected	49	47	38	75	44	62

Licensed Cell Type by Species

Bovine	**Equine**	**Porcine**	**Feline**	**Canine**
MDBK Turbinate Kidney	Kidney Dermis	Kidney PK-15 PK-2a Testis	Fetal Heart Emb. Lung CRFK	Kidney MDCK NLDK Macrophage Histiocyte Bone Marrow
Monkey	**Hamster**	**Mouse**	**Ovine/Caprine**	**Avian**
Vero MA-104 BS C-1 BGM	CHO BHK21	Macrophage Hybridomas McCoy	Lamb Kidney Goat Kidney	Hep. Carcinoma Thymocytes RP-19 QT-35
Insect	**Human**	**Misc.**		
T. ni Tick Sf21 Sf9	Rectal Tumor Lung	CHSE Bat Lung Rat Kidney		

Discussion: Serum Virus Risk

- **Bovine**

  Encephalitis, BSE, VSV, Bov Herpes 4
- **Porcine**

  Porcine circo, Japanese B enceph, Hepatitis E, ASF, PRRS,
- **Equine**

  WNV, encephalitis, VSV

Zoonotic diseases & considerations

Virus Type	Primary host / vector	Disease in humans
Eastern Encephalitis	Horses / mosquitoes	Encephalomyelitis
Western Encephalitis	Horses / mosquitoes	Encephalomyelitis
Venezuelan Encephalitis	Horses / mosquitoes	Encephalitis
Japanese B Encephalitis	Horses,cattle,pigs	Encephalomyelitis
Tick borne Encephalitis	Cattle,goats / ticks	Encephalitis
California Encephalitis	Horses,cattle / mosquitoes	Encephalitis
Rabies	Cattle	Paralysis,death
Prions	Cattle, sheep	
Bovine spongiform Encephalopathy	Cattle	Atypical Creutzfeldt-Jakob Disease
Vaccinia	Cattle,horses	Skin lesions
Bovine pustular Stomatitis virus	Sheep,goats	Skin lesions
Vesicular Stomatitis	Cattle,swine,horses	Fever,chills, headache
Parainfluenza 3	Cattle	Flu-like symptoms
Rift Valley Fever	Cattle,sheep	Fever, influenza-like symptoms, death

Conclusions

- Risks
  - Contaminated cell cultures
  - Contaminated cell & virus stocks
  - Contaminated vaccines
  - Contaminated transplants
  - In vitro fertilization problems
  - Missed diagnostic tests

Conclusions

- Remedies
  - Continued testing
  - Test method improvement
  - Serum free media research
  - Sourcing
  - Viral inactivation methods

Conclusions

Results

- Pure, safe, potent and effective vaccines
- Correct diagnostic results
- Accidental infection of inoculated animals and zoonotics traced to vaccines will not occur